Medical Policy Manual Surgery, Policy No. 213

Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy of Intracranial, Skull Base, and Orbital Sites

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Stereotactic radiosurgery (SRS) and stereotactic body radiotherapy (SBRT) or stereotactic ablative radiotherapy (SABR) are radiotherapy techniques that use highly focused radiation beams to treat both neoplastic and non-neoplastic conditions, in contrast to traditional external radiation beam therapy, which involves the use of relatively broad fields of radiation over a number of sessions that may occur over weeks to months.

MEDICAL POLICY CRITERIA

Note: Clinical documentation to support criteria is required (See Required Documentation).

Medically Necessary

I. Stereotactic radiosurgery (SRS) and stereotactic body radiation therapy (SBRT), also known as stereotactic ablative body radiotherapy (SABR), may be considered **medically necessary** for initial treatment or treatment of recurrence for any of the following indications:

A. Primary neoplasms of the central nervous system (CNS) (see Policy Appendix I), including but not limited to low grade gliomas and high-grade gliomas

B. Metastatic lesion(s) to the CNS (solitary or multiple) in individuals with a current Karnofsky performance score greater than or equal to 60 or a current ECOG score less than or equal to 2 (see Policy Guidelines)

C. Arteriovenous malformations

D. Intracranial cavernous malformation

E. Chordomas and chondrosarcomas of the skull base

F. Craniopharyngiomas

G. Refractory epilepsy when all of the following criteria are met:

1. Any seizure activity despite treatment with at least two antiepileptic regimens; and
2. Documentation of clinical agreement of medical appropriateness from a neurosurgeon or multidisciplinary body of physician consultants.

H. Essential tremor or Parkinson's disease when all of the following criteria are met:

1. Symptoms are ongoing despite treatment with at least two drug regimens; and
2. Documentation of clinical agreement of medical appropriateness from a neurosurgeon or multidisciplinary body of physician consultants.

I. Head and neck cancers within intracranial, skull base, and orbital sites, when there is documented prior radiation treatment to the planned target volume

J. Hemangioblastoma within intracranial, skull base, and orbital sites

K. Hemangiopericytoma within intracranial, skull base, and orbital sites

L. Glomus jugulare and glomus tympanicum tumors

M. Meningiomas, benign, atypical, or malignant

N. Pituitary adenomas

O. Schwannomas (see Policy Guidelines)

P. Trigeminal neuralgia (tic douloureux) refractory to medical management

Q. Uveal melanoma

Investigational

II. SRX and SBRT (also known as SABR) are considered **investigational** when Criterion I. is not met and for all other intracranial, skull base, and orbital indications including but not limited to choroidal neovascularization (CNV), chronic pain, and functional disorders other than trigeminal neuralgia and essential tremor.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

POLICY GUIDELINES

For the purposes of this policy, neoplasm is defined as “an abnormal mass of tissue that

results when cells divide more than they should or do not die when they should. Neoplasms may be benign (not cancer), or malignant (cancer)."[1]

ARTERIOVENOUS MALFORMATION

Subcategories of arteriovenous malformation include dural arteriovenous fistula, also known as dural arteriovenous malformation.

SCHWANNOMAS

Schwannomas are tumors that occur along nerves. They are typically benign but may be malignant. These may also be referred to as neuromas, neurinomas "of Verocay" or neurilemmomas. A common type of schwannoma is a vestibular schwannoma, which is also known as an acoustic neuroma.

PERFORMANCE STATUS MEASUREMENT

Performance status is frequently used in oncology practice as a variable in determining prognosis and management strategies. Either the Karnofsky Performance Status (KPS) or the Eastern Cooperative Oncology Group (ECOG) Performance Status scoring systems may be used.

Karnofsky Performance Status

100	Normal, without symptoms
90	Able to carry on normal activity; minor signs or symptoms of disease
80	Normal activity with effort; some signs or symptoms of disease
70	Cares for self; unable to carry on normal activity or do active work
60	Requires occasional assistance; able to care for most personal needs
50	Requires considerable assistance and frequent medical care
40	Disabled; requires special care and assistance
30	Severely disabled; hospitalization is indicated
20	Very sick; active support treatment is necessary
10	Moribund; fatal processes progressing rapidly

ECOG Performance Status

0	Fully active, able to carry on all pre-disease performance without restriction.
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.
2	Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours.
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours.
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair.

FRACTIONATION

Fractionated stereotactic radiotherapy refers to SRS or SBRT being performed more than once on a specific site. SRS is commonly delivered in one fraction and SBRT or SABR is commonly delivered in two to five fractions.

DOSE CONSTRAINT REFERENCES

Radiation Therapy Oncology Group (RTOG) Radiation Dose Constraints

Available from: https://en.wikibooks.org/wiki/Radiation_Oncology/Toxicity/RTOG

Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC)

Available from: https://en.wikibooks.org/wiki/Radiation_Oncology/Toxicity/QUANTEC

REQUIRED DOCUMENTATION

The information below **must** be submitted for review to determine whether policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

- History/Physical and Chart notes, including requirements as outlined by the policy criteria, as applicable to the indication for treatment.
- As applicable, documentation of sites, size and number of lesions
- As applicable, documented ECOG score or Karnofsky performance score

CROSS REFERENCES

1. Charged-Particle (Proton) Radiotherapy, Medicine, Policy No. 49
2. Intensity Modulated Radiotherapy (IMRT) of the Central Nervous System (CNS), Head, Neck, and Thyroid, Medicine, Policy No. 164
3. Intensity Modulated Radiotherapy (IMRT) of the Thorax, Abdomen, Pelvis, and Extremities, Medicine, Policy No. 165
4. Intensity Modulated Radiotherapy (IMRT) for Breast Cancer, Medicine, Policy No. 166
5. Intensity Modulated Radiotherapy (IMRT) for Tumors in Close Proximity to Organs at Risk, Medicine, Policy No. 167
6. Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy for Tumors Outside of Intracranial, Skull Base, or Orbital Sites, Surgery, Policy No. 214
7. Responsive Neurostimulation, Surgery, Policy No. 216

BACKGROUND

Stereotactic radiosurgery (SRS) and stereotactic body radiation therapy (SBRT) rely on three-dimensional imaging to localize the therapy target. SRS and SRBT have been used for a range of malignant and non-malignant conditions. Because they are more targeted than traditional external radiation therapy, SRS and SRBT are often used for treatment at sites that are difficult to reach via surgery, located close to other vital structures, or subject to movement within the body. The term SBRT will be used to describe treatment also referred to as stereotactic ablative body radiotherapy (SABR).

SRS and SBRT (or SABR) employ similar technological "stereotactic" sophistication with elements of advanced pretreatment imaging for localization of target(s), patient immobilization, control of breathing associated tumor movement, focally targeted treatment planning, and daily image guidance to ensure precise delivery of high daily doses of radiation. As commonly used in the medical literature, SRS refers to intracranial treatments and SBRT refers to extracranial treatments. Alternatively, SRS and SBRT may be defined independent of whether treatment is directed to intra or extra cranial tumors volumes. According to this definition, when such treatment is given as a single fraction, it may be referred to as SRS, and when it is delivered in two to five fractions it may be referred to as SBRT or SABR.

The fractionation used for SRS and SBRT is referred to as “hypofractionated” because it is fewer treatments than those used for conventional external beam radiotherapy.” Fractionation of stereotactic radiotherapy aims to optimize the therapeutic ratio; that is the ratio between tumor control and late effects on normal tissues. The main advantage of fractionation is that it allows higher total doses to be delivered to the tumor because of increased tolerance of the surrounding healthy tissues to each individual, fractionated dose. In addition, some lesions such as large arteriovenous malformations may require more than one procedure to complete the obliteration process.

SRS and SBRT can be administered by several types of devices that are distinguished by their source of radiation, including particle beams (e.g., proton), gamma radiation from cobalt-60 sources, or high-energy photons from linear accelerator (LINAC) systems. The Gamma Knife and linear accelerator systems (including the Cyberknife®) are similar in concept; both use multiple photon radiation beams that intersect at a stereotactically determined target, thus permitting higher doses of radiation delivery with sparing of surrounding normal tissues. The differences between the two relate to how the energy is produced (i.e., through decaying cobalt-60 in the gamma knife devices, or from x-rays in the linear accelerator system) and the number of energy sources used (i.e., multiple energy sources in the gamma knife versus one in the linear accelerator system).

IMAGE-GUIDED RADIOSURGERY OR RADIOTHERAPY

Image-guided radiosurgery or radiotherapy is a relatively new development collectively describing units with real-time image guidance systems. Examples include the Cyberknife® device, BrainLAB Novalis®, TomoTherapy®, and LINAC with computerized tomography (CT).

REGULATORY STATUS

Several devices that use cobalt 60 radiation (gamma ray devices) for SRS have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. The most commonly used gamma ray device is the GammaKnife (Elekta; approved May 1999). Gamma ray emitting devices that use cobalt 60 degradation are also regulated through the U.S. Nuclear Regulatory Commission.

A number of LINAC movable platforms that generate high-energy photons have been cleared for marketing by the FDA through the 510(k) premarket notification process including the Novalis Tx®

(Novalis, Westchester, IL); the TrueBeam STx (Varian Medical Systems, Palo Alto, CA, approved December 2012); and the CyberKnife® System (Accuray, Inc.; approved December 1998). LINAC-based devices may be used for intracranial and extracranial lesions.

Note: Particle radiation can also be used without stereotactic guidance. In this setting, the use of particles is referred to as proton, helium, or neutron radiation *therapy*. Proton or helium ion radiation therapies (RT), intraocular RT for age-related macular degeneration, and electromagnetic navigation bronchoscopy for placement of fiducial markers are considered in separate medical policies. See cross-reference section below.

EVIDENCE SUMMARY

The selection of variables used in the delivery of SRS and SBRT is complex and individualized, requiring selection of the device, radiation dose, and the size and shape of

treatment margins All of these variables depend on the location, shape, and radiosensitivity of the target tissue and the function and radiosensitivity of the surrounding tissue. Trials that allow direct comparison of all of the possible variables involved in selecting specific SRS and SBRT methods do not broadly exist making it difficult to draw comparative effectiveness conclusions. Further, for many rare conditions, large comparative studies are unlikely. The evidence below will focus on indications with criteria and investigational indications.

Please note that the evidence review below does not compare specific radiation planning and delivery techniques.

TRIGEMINAL NEURALGIA

Tuleasca published a 2018 systematic review of SRS for trigeminal neuralgia to support the development of a guideline endorsed by the International Society of Stereotactic Radiosurgery (ISRS). A total of 65 studies met inclusion criteria, with a total of 6461 patients. One study was prospective and the remainder were retrospective. Crude rates of hypesthesia ranged from 0% to 68.8% (mean 21.7%, median 19%) for gamma knife surgery (GKS), from 11.4% to 49.7% (mean 27.6%, median 28.5%) for LINAC, and from 11.8% to 51.2% (mean 29.1%, median 18.7%) for CyberKnife radiosurgery. Other toxicities reported were dysesthesias, paresthesias, dry eye, deafferentation pain, and keratitis. Actuarial initial freedom from pain without medication was reported to be 28.6% to 100% (mean 53.1%, median 52.1%), 17.3% to 76% (mean 49.3%, median 43.2%), and 40% to 72% (mean 56.3%, median 58%) for GKS, LINAC, and CyberKnife radiosurgery, respectively. Recurrence rates were reported as ranges of 0 to 52.2% (mean 24.6%, median 23%), 19% to 63% (mean 32.2%, median 29%), and 15.8% to 33% (mean 25.8%, median 27.2%) for GKS, LINAC, and CyberKnife radiosurgery, respectively. The authors concluded that although the evidence is limited, radiosurgery is a safe and effective therapy for drug-resistant trigeminal neuralgia.

In 2017, Gubian and Rosahl published a meta-analysis of the safety and efficacy of SRS and microsurgery for trigeminal neuralgia. PRISMA guidelines were followed. A total of 53 studies met inclusion criteria. Success rates initially and at last follow-up (>five years after intervention) were 71.1% and 63.8% for SRS and 86.9% and 84% for microsurgery, respectively. Mean percentage of recurrence at 36-months post-intervention was 25% for SRS and 11% for microsurgery (p=0.0015). The length of recurrence-free intervals was not significantly different between SRS and microsurgery (30.45 and 30.55 months, respectively, p=0.987). The difference in incidence of hearing loss was also not significant (SRS 1.51% vs microsurgery 0.74%), but facial dysesthesia was more frequent in the SRS group (2.3% versus 28.8% for microsurgery, p=0.02).

A 2011 Cochrane systematic review of 11 trials of neurosurgical interventions for trigeminal neuralgia found that there was very low-quality evidence for the efficacy of most neurosurgical procedures for trigeminal neuralgia because of the poor quality of the trials.[2] All procedures produced variable pain relief, but many resulted in sensory side effects. There were no studies of microvascular decompression which observational data suggests gives the longest pain relief. Only one study was identified that used radiosurgery. The trial was intended to determine if increasing the nerve length within the SRS treatment volume would change outcomes. The study was stopped before accrual was completed and it was noted that pain measurements using validated scales were not made either before or after surgery.

Other nonrandomized studies and case series have reported on the use of SRS for trigeminal neuralgia.[3-8]

Section Summary

Case series identify improvements in pain related to trigeminal neuralgia after treatment with SRS. Comparative studies that evaluate the use of SRS compared with alternative treatments for trigeminal neuralgia are lacking. Only one study specifically addressed the use of radiosurgery and it was stopped before accrual was completed.

REFRACTORY EPILEPSY

Barbaro (2018) published the results of the first randomized controlled trial comparing SRS for the treatment of pharmacoresistant unilateral mesial temporal lobe epilepsy to anterior temporal lobectomy (ATL), the ROSE trial.[9] A total of 37 (64%) patients achieved seizure remission, with 16 (52%) in SRS and 21 (78%) in ATL. Noninferiority of SRS compared to ATL was not demonstrated. SRS did not confer sparing of verbal memory deficits compared to ATL. QOL scores improved significantly in the SRS group at 24 months and remained steady at 36 months, in contrast to the ATL group in whom QOL score improvement was immediately noticeable at 12 months. Adverse events were anticipated cerebral edema and related symptoms for some SRS patients, and cerebritis, subdural hematoma, and others for ATL patients. These all resolved with appropriate protocol specified interventions.

Quigg (2018) published a follow-up report on visual field defects (VFD) observed in patients treated during the ROSE trial.[10] Out of 58 treated patients, 29/31 (93.5%) SRS patients and 25/27 (92.6%) ATL patients completed visual field testing. Ninety-three percent of patients treated with SRS reported VFD compared to 88% of patients treated with ATL (p=0.65). Younger age at diagnosis correlated with worse outcomes; this significance was stronger in the SRS arm compared to the ATL arm (p=0.04 and 0.20), but this difference was not significant upon multivariable regression. Presence or absence of VFD was not correlated with either seizure remission (p=0.22 and p=1.00) or driving status (p=0.53 and p=1.00) for the SRS or ATL treatment arms, respectively.

A 2018 systematic review by Eekers reported on 16 studies including a total of 170 patients.[11] Methodological quality of the included studies was graded using a modified QUADAS checklist. Limitations of the reviewed studies include a lack of control groups and poorly defined exclusion criteria. SRS was reported to have a positive effect on seizure outcome, defined as the total percentage of radiotherapy-adapted Engel class (RAEC) I and II patients, in 12 studies. No favorable effect on seizure outcome was found in two studies, although these contained only two and three patients, respectively. Toxicities reported include radionecrosis, impaired cognitive functioning, and headache, nausea, and vomiting related to increased intracranial pressure and edema. Subsequent resection was reported in nine of the studies. In those studies, 20% of patients underwent subsequent resection. Reasons reported were persisting seizures, cyst formation, edema, intracranial hypertension, and radionecrosis. Authors concluded that there is only level 4 evidence of primary radiotherapy reducing seizure frequency in adult patients and that prospective randomized trials are needed to determine its value.

McGonigal (2017) performed a systematic review of SRS for drug-resistant epilepsy and assessed the level of evidence according to the PRISMA guidelines.[12] A total of 55 articles met inclusion criteria. Level 2 evidence (prospective studies) indicated that SRS may result in superior neuropsychological outcomes and quality of life compared to microsurgery for mesial temporal lobe epilepsy and that SRS has a better risk-benefit ratio for small hypothalamic hamartomas compared to surgical methods. Only Level 4 evidence (case reports, prospective

observational studies, and retrospective case series) was available for the other indications and no Level 1 evidence was identified.

In 2016, Feng published a systematic review and meta-analysis of data from 13 studies on the use of SRS to treat mesial temporal lobe epilepsy.[13] They calculated approximately half of the patients were seizure free over a follow-up period that ranged from six months to nine years (pooled estimate, 50.9%, 95% CI, 38.1% to 63.6%), with an average of 14 months to seizure cessation (pooled estimate 14.08 months, 95% CI, 11.95 to 12.22 months). Nine of 13 included studies reported data for adverse events, which included visual field deficits and headache (the two most common adverse events), verbal memory impairment, psychosis, psychogenic nonepileptic seizures, and dysphasia. Patients in the individual studies experienced adverse events at rates that ranged from 8% for nonepileptic seizures to 85% for headache.

A 1998 TEC Assessment[14] cited two studies of 11 and 9 patients, respectively, in which radiosurgery was used to treat epilepsy. The subsequent literature search revealed three small studies on the use of radiosurgery for medically refractory epilepsy. Regis (2000)[15] selected 25 patients with mesial temporal lobe epilepsy, 16 of whom provided minimum two-year follow-up. Seizure-free status was achieved in 13 patients, two patients were improved, and three patients had radiosurgery-related visual field defects.

A study by Schrottner (1998)[16] included 26 patients with tumor-related epilepsy, associated mainly with low-grade astrocytomas. Mean follow-up among 24 available patients was 2.25 years. Tumor location varied across patients. Seizures were simple partial in six (three with generalization) and complex partial in 18 (five with generalization, one gelastic). Seizures were eliminated or nearly so in 13 patients. Little improvement was observed in four patients and none in seven. Whang and Kwon (1996)[17] performed radiosurgery in 31 patients with epilepsy associated with nonprogressive lesions. A minimum of one-year follow-up was available in 23 patients, 12 of whom were seizure-free (and three of whom had antiseizure medications discontinued), two had seizures reduced in frequency, and nine experienced no change. While the Regis series selected a fairly homogeneous clinical sample, the other two studies were heterogeneous.

Section Summary

For individuals with epilepsy refractory to medical management, the evidence on the use of SRS as a treatment for epilepsy includes case reports in primary epileptic disorders and case reports for tumor-related epilepsy. For mesial temporal lobe epilepsy, there is a pilot prospective non-comparative intervention and a single RCT comparing SRS to anterior temporal lobectomy (ATL).

TREMOR AND PARKINSON DISEASE

SRS has been used for the treatment of tremor via stereotactic radiofrequency thalamotomy.

Martínez-Moreno published a systematic review of stereotactic radiosurgery for tremor in association with International Stereotactic Radiosurgery Society practice guidelines.[18] The systematic review was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria. A total of 34 studies met inclusion criteria. Of these, 30 were retrospective noncomparative studies and 14 studies had fewer than 10 patients. Three studies were prospective and one was a retrospective comparative study.

Rates of tremor reduction were similar across the included studies, with an average of 88%. The one comparative study reported similar tremor control rates between SRS, deep brain stimulation, and radiofrequency thermocoagulation. There were fewer permanent complications and longer latency to clinical response following SRS than the two other modalities. The authors concluded based on level IV evidence that SRS for tremor is well-tolerated and effective.

Dallapiazza (2018) conducted a systematic review comparing the outcomes of various surgical procedures for the treatment of refractory essential tremor, including deep brain stimulation (DBS), thalamotomy with radiofrequency (RF), SRS, and focused ultrasound (FUS).[19] Studies were pooled and graded for their overall level of evidence according to the Oxford Centre for Evidence-based Medicine standards. Measured outcomes included tremor control according to the Fahn-Tolosa-Marin (FTM) rating scale, quality of life (QOL) improvements, and complication rates. Overall, while complication rates were generally lower for SRS compared to other interventions, alternative approaches presented higher control rates and QOL improvements at more robust tiers of evidence.

Raju (2017) assessed outcomes of SRS for medically refractory tremor associated with Parkinson disease (PD) in a retrospective analysis of 33 patients.[20] All patients underwent gamma knife thalamotomy. Median follow-up was 23 months (range, 9 to 144 months). A total of 31 patients (93.9%) experienced improvements in tremor and 23 patients (70.0%) had complete or nearly complete tremor arrest. Improvements in other PD symptoms were also observed, including one patient (3%) with improvements in bradykinesia, three patients (9%) with improvements in rigidity, and three patients (9%) who reduced their dosage of dopa after SRS.

Section Summary

The evidence related to the use of SRS for tremor consists of uncontrolled cohort studies, many of which report outcomes from the treatment of tremor of varying etiologies. Most studies report improvements in standardized tremor scores, although few studies used a blinded evaluation of tremor score, allowing for bias in assessment. No studies that compared SRS with alternative methods of treatment or a control group were identified. Limited long-term follow-up is available, making the long-term risk: benefit ratio of an invasive therapy uncertain.

CHRONIC PAIN

A 2022 systematic review published by Franzini evaluated medial thalamotomy using SRS for the treatment of intractable pain.[21] A total of six studies met inclusion criteria. There was some overlap with the Roberts and Pouratian systematic review below, but three included studied were published after the publication of the previous review. Across the six studies, 125 patients were treated with SRS and 118 were included in the outcome analysis. Meaningful pain reduction was reported in 55% of patients overall (with 38% persisting to last follow-up) and 43.3 to 100% per study. Adverse events were reported in six patients (5%).

Lu (2018) reported a systematic review and meta-analysis of neurosurgical treatments for glossopharyngeal neuralgia.[22] A total of 23 studies were included on nerve section (NS,, six studies), microvascular decompression (MVD, 11 studies), and SRS (six studies). The meta-analysis indicated that short-term and long-term pain relief indicence rate was highest after NS (94% 95% confidence interval [CI] 88% to 98%; 96%, 95% CI 91% to 99%). The short-term and long-term pain relief incidence rate was lowest after SRS (three months postoperatively

80%, 95% CI 68% to 96%; 82%, 95% CI 67% to 94%). The postoperative complication indicence rate was highest and lowest following MVD (26%, 95% CI 16% to 38%) and SRS (0%, 95% CI 0% to 4%), respectively.

In 2017, Roberts and Pouratian performed a systematic review to evaluate the efficacy of SRS for chronic pain.[23] They identified six articles with 113 patients that underwent SRS and had at least a three month follow-up for nonmalignant pain or at least a one month follow-up for malignant pain. At least 35% of patients reported having significant pain relief, but 21% of patients reported adverse events.

Section Summary

The evidence related to the use of SRS for chronic pain is limited and there remains a lack of comparative studies and long-term outcomes. This evidence is not sufficient to understand the safety and effectiveness of SBRT for the treatment of chronic pain or to adequately describe the subpopulation of patients with chronic pain most likely to benefit.

BRAIN METASTASES

Systematic Reviews

A systematic review and meta-analysis by Pichardo-Rojas (2026) compared SRS alone to SRS plus whole brain radiation therapy (WBRT).[24] The review included six cohort studies and four RCTs. No significant differences were found between treatments for overall survival, radionecrosis, or local tumor control. Recurrence rates were lower for SRS plus WBRT (13.9% vs. 37%, p=0.0005), but the combined treatment was also associated with neurocognitive deterioration greater than or equal to one standard deviation from baseline.

Garsa (2021) conducted a systematic review of available evidence comparing WBRT and SRS alone or in combination, as initial or postoperative treatment, with or without systemic therapy for adults with brain metastases due to lung cancer, breast cancer, or melanoma.[25] Despite the identification of 97 studies, statistical analyses were limited due to heterogeneity across the available data. Based on pooled data from four RCTs, there was no statistically significant difference in overall survival (OS) when comparing SRS plus WBRT to SRS alone or to WBRT alone (hazard ratio [HR] 1.09, 95% CI 0.69 to 1.73). Based on pooled data from three RCTs, OS did not differ when comparing postsurgical WBRT to postsurgical SRS (HR 1.17, 95% CI 0.61 to 2.25). Lastly, pooled data from four RCTs did not show a significant difference in the risk of serious adverse events with WBRT plus SRS versus WBRT or SRS alone (relative risk [RR] 1.05, 95% CI 0.12 to 8.89).

Chen (2021) published a systematic review of the use of SRS for brainstem metastases.[26] A total of 32 studies, all retrospective, including 1,446 patients, met inclusion criteria. Heterogeneity across studies was low to moderate (median I^2=35%, range 30 to 62%). No significant publication bias was identified. According to the meta-analyses, the one-year local control was 86% (95% CI 83 to 88%) based on 31 studies, the objective response rate was 59% (95% CI 47 to 71%) based on 17 studies, and the rate of symptom improvement was 55% (95% CI 47 to 63%) based on 13 studies. Deaths from brainstem metastases progression following SRS occurred in 19 patients across the 19 reporting studies. Grade 3 to 4 toxicities occurred in 2.4% (95% CI 1.5 to 8.7%) of patients.

An Agency for Healthcare Research and Quality Comparative Effectiveness Review of radiation therapy for brain metastases was published in 2020.[27] The review included

randomized controlled trials and large observational studies of WBRT and SRS alone or in combination. These were used as initial or postoperative treatment and with or without systemic therapy. A total of 91 studies met inclusion criteria. These included 60 RCTs that addressed WBRT and 13 RCTs that addressed SRS. For SRS, the authors deemed the evidence insufficient for assessing overall survival, disease-free survival, deaths due to brain metastases, intracranial progression, functional status, and cognitive effects. Differences reported include a statistically significant difference between WBRT using radiosensitizers and WBRT alone, with improved survival associated with the addition of radiosensitizers (HR 0.87, 95% CI 0.83 to 0.90; three RCTs; moderate strength of evidence). Most outcomes were not different between these groups. These included quality of life, which was not different between patients receiving SRS plus WBRT and patients receiving SRS alone, overall survival, which was not different between surgery plus radiation therapy and surgery alone, and serious adverse events, adverse events, radiation necrosis, fatigue, and seizures, for which there were systemic differences across interventions. The risk of dying from brain metastases was numerically but not statistically different in favor of radiation post-surgery versus surgery alone (RR 0.64, CI 0.22 to 1.84, three RCTs, low strength of evidence).

Liu (2020) conducted a systematic review to compare SRS to surgical resection in the initial treatment of brain metastases.[28] The review included 20 studies (18 retrospective cohorts; 2 RCTs) involving 1,809 patients. Results revealed that SRS and surgical resection were comparable with regard to local control (HR 1.02, 95% CI 0.64 to 1.64, p=0.92), distant intracranial control (HR 0.78, 95% CI 0.38 to 1.60, p=0.49), and OS (HR 0.91, 95% CI 0.65 to 1.27; p=0.57) in patients with single or solitary brain metastases. However, the authors noted that a prospective RCT with a larger patient population and a longer follow-up is necessary to confirm their findings.

Loi (2020) published a systematic review of SRS for local failure following SRS of brain metastases.[29] Eleven studies with a total of 335 patients met inclusion criteria. The pooled one-year local failure and median OS were 24% (95% CI 19 to 30%) and 14 months (95% CI 8.8 to 22.0%), respectively. The cumulative crude radionecrosis rate was 13% (95% CI 8 to 19%). According to a subgroup analysis, higher incidence of radionecrosis occurred in studies with median patient age of 59 years and above (13% [95% CI 8 to 19%] vs 7% [95% CI 3 to 12%], p=0.004), while lower radionecrosis incidence occurred following prior While Brain Radiotherapy (WBRT 19%, 95% CI 13 to 25%; vs 7%, 95% CI 30 to 13%, p=0.004). Heterogeneity was reported as acceptable.

Fuentes (2018) published a systematic review of RCTs to compare surgery with SRS for patients with a single brain metastasis.[30] Risk of bias was assessed with the Cochrane tool. Two RCTs met inclusion criteria. These included 85 patients. Both included studies were closed early due to poor participant accrual. Meta-analysis was not possible due to heterogeneity between the studies. Certainty of evidence was rated as low or very low for the various outcomes. Neither RCT reported differences in overall survival between the interventions. There were also no differences in progression-free survival, quality of life, or adverse events.

Khan (2017) published a meta-analysis of comparing WBRT, SRS, and treatment with a combination of the two for brain metastases.[31] Five studies with a total of 763 patients met inclusion criteria and were included in the meta-analysis. Out of those, 26% received WBRT alone, 26% received SRS alone, and 48% received WBRT plus SRS. No significant differences between treatment groups were found for survival benefit or adverse events.

However, combination therapy provided significantly better local control than WBRT alone (HR 2.05, 95% CI 1.36 to 3.09, p=0.0006) or SRS alone (hazard ratio 1.84, 95% CI: 1.26 to 2.70, p=0.002).

In 2017, Ghidini conducted a systematic review on CNS metastases from esophageal and gastric cancer.[32] The authors analyzed data from 37 studies that met the criteria for inclusion. SRS was found to result in better OS, with the caveat that the studies examined included combination therapies that could cause an overestimate of survival.

Randomized Controlled Trials

Since the systematic reviews above, Yadav (2026) published an open-label RCT comparing SRS to WBRT in 103 breast cancer patients with one to five brain metastases. After a median follow-up of 17.5 months, there were no significant differences between the groups for most outcome measures, including overall survival and median progression-free survival.[33]

Nonrandomized Comparative Studies

Verma (2013) retrospectively reviewed patients receiving different radiotherapy modalities for brain metastases with or without tyrosine kinase inhibitor (TKI) therapy.[34] Among 34 patients (89 lesions) those receiving SRS and TKIs had six-month local control rates of 94.7% vs 73.7% in the group who received SRS without TKIs. The difference was not statistically significant (p=0.09).

Tian (2013) reported results from a retrospective, single-institution cohort study comparing neurosurgical resection to SRS for solitary brain metastases from non-small-cell lung cancer (NSCLC). Seventy-six patients were included, 38 of whom underwent neurosurgery.[35] Median survival was 14.2 months for the SRS group and 10.7 months for the neurosurgery group. In multivariable analysis, treatment mode was not significantly associated with differences in OS.

Noncomparative Studies

Noncomparative studies continue to evaluate the use of SRS without WBRT for the management of brain metastases and the role of SRS for the management of larger numbers of brain metastases.[36-42]

Section Summary

For cases of brain metastases, evidence from RCTs, nonrandomized studies, and systematic reviews indicate that the use of SRS improves outcomes in the treatment of brain metastases. SRS appears to be feasible in the treatment of larger numbers (e.g., >10) of brain metastases, and outcomes after SRS treatment do not appear to be worse for patients with larger numbers of metastases, at least for patients with 10 or fewer metastases.

CAVERNOUS MALFORMATIONS

Systematic Reviews

The International Stereotactic Radiosurgery Society (2024) conducted a systematic review and meta-analysis to establish evidence-based guidelines for single-fraction SRS in treating intracranial cavernous malformations (CM).[43] The meta-analysis included 32 studies (n=2672) and showed a decrease in annual hemorrhage rates post-treatment (RR: 0.17), in the first 2 year (RR: 0.29), and after 2 years (RR: 0.11). Hemorrhage rates differed before and after 2

years post-SRS (RR: 0.36). Among epileptic patients, 20.2% had epilepsy pretreatment, and 49.9% were seizure-free post-SRS, while 30.6% experienced reduced seizure frequency. Lesion volume changes showed a reduction in 46.9%, stability in 47.1%, and an increase in 6.7%. Symptomatic radiation effects occurred in 8% of patients, with symptomatic change rates of 6% at doses ≤13 Gy compared to 9% at doses >13 Gy. Permanent clinical deficits were rare (2%). The authors conclude SRS can be an effective intervention for intracranial cavernous malformations, reducing hemorrhage rates and improving seizure outcomes.

Tos (2024) published a systematic review and meta-analysis to determine outcomes of SRS for deep-seated (brainstem, basal ganglia, thalamus, cerebellar peduncle) intracranial CM.[44] The review included 14 studies with 850 participants diagnosed with deep-seated CM. Outcomes of interest were annual hemorrhage rate, lesional volume change, and radiation-induced changes. All 14 studies involved 10 or more subjects, and 12 were single institution reports. One study was a prospective observation trial; 12 studies were retrospective cohorts, and one was a case-control study. Median follow-up range was 32 to 121.9 months. Compared to pre-SRS, the pooled risk ratio (RR) for annual hemorrhage rate was 0.13 (95% CI 0.11-0.16, p<0.0001), indicating reduced hemorrhage rates after SRS. In study subsets, lesion volume was reduced in 204/461 participants (44.25%, 10 studies) and lesion volume stability was seen in 170/303 participants (56.1%, 8 studies). Increase in lesion volume was reported in 7/303 participants, however, it was not clear from most studies whether reported increases were due to lesion progression, radiation-induced changes, or hemorrhage. The pooled incidence of symptomatic radiation-induced changes was 9%. Limitations include that the studies do not confirm whether the deep-seated CMs were inoperable; the studies lack comparators and are primarily retrospective. Other limitations include inconsistent treatment and outcome reporting.

Gao (2021) published a systematic review comparing microsurgery and gamma knife radiosurgery for the treatment of brainstem cavernous malformations.[45] Cohort studies reporting on 20 or more patients of any age with brainstem cavernous malformations with at least 80% completeness of follow-up were included, resulting in an analysis of 43 cohorts with 2,492 patients. Rehemorrhage rates were reduced by both microsurgery (RR=0.04, 95% CI 0.01 to 0.16, p<0.01) and radiosurgery (RR 0.11, 95% CI 0.08 to 0.16, p<0.01). The difference in median number of patients experiencing symptomatic intracranial hemorrhage between groups was statistically significant (microsurgery median 0, range 0 to 33; radiosurgery median 4, range 1 to 14, p<0.05). Persistent focal neurological deficit was also significantly different between groups (neurosurgery median 5, range 0 to 140; radiosurgery median 1, range 0 to 3; p<0.05).

Poorthuis (2019) performed a systematic review of SRS for cerebral cavernous malformations.[46] A total of 30 studies met inclusion criteria. The median follow-up was 48 months. The annual incidence of death, intracerebral hemorrhage, and nonhemorrhagic persistent focal neurological deficit were 0.18% (95% CI 0.10 to 0.31), 2.40% (95% CI 2.05 to 2.80), and 0.71% (95% CI 0.53 to 0.96), respectively. The composite index including the incidence of all of these outcomes was 3.63% (95% CI 3.17 to 4.16).

Kim (2019) performed a systematic review of outcomes following SRS for brainstem cavernous malformations.[47] A total of 14 studies with 576 patients met inclusion criteria and were included in a meta-analysis. The hemorrhage rate was significantly lower post-SRS versus pre-SRS (pooled incidence rate ratio [IRR] 0.123, p<0.001) and two-years post-SRS versus within two years after SRS (IRR 0.317, p<0.001). At last follow-up, lesion volume was reduced in 47.3% of patients and unchanged in 49.4%. Symptomatic adverse radiation effects were

reported in 7.3% of patients, with 2.2% of patients reporting permanent adverse radiation effects.

Wen (2019) performed a systematic review and meta-analysis of gamma knife radiosurgery for cavernous malformations.[48] A total of nine studies met inclusion criteria, representing 747 patients. All studies were retrospective, and one was case-controlled. The authors calculated the overall risk ratio (RR) of hemorrhage rate of pre-GKRS and post-GKRS (6.08, 95% CI 5.04 to 7.35), the RR comparing hemorrhage rate of pre-GKRS and the first two years post-radiosurgery (3.03, 95% CI 2.65 to 4.11), and the overall RR (12.13, 95% CI 1.73 to 85.07) comparing pre-GKRS with two years after GKRS. There was no significant difference of the hemorrhage rate between the first two years following treatment and two years after treatment (RR=2.81; 95% CI 0.20 to 13.42). Adverse events reported in eight of the studies were cyst formation, edema, new lesions, and neurologic deficiency.

Non-randomized studies

Li (2025) conducted a prospective cohort study that compared SRS for brainstem CM to observation in 377 participants from 17 hospitals.[49] Study subjects were consecutively enrolled, with a 3:1 ratio of observation (n=280) vs SRS (n=97). There were no significant differences in baseline characteristics. After a median follow-up of 70 months, 70 (25.0%) of the observation group experienced hemorrhage vs. 10 (10.3%) of the SRS group. SRS was found to be an independent protective factor against hemorrhage (HR= 0.379, 95% CI 0.195 to 0.738, p=0.004). Twelve participants (12.4%) experienced adverse effects from radiation with no permanent effects. New or worsening neurological dysfunction was significantly higher in the observation group (28.9%) compared to the SRS group (16.5%; p=0.016). Limitations of the study include lack of randomization, potential selection bias, and hospital-specific differences in expertise and radiologic interpretations. The authors concluded that SRS is associated with improved hemorrhage-free survival in people with brainstem CM.

Dayawansa (2024) published an international retrospective review examining sSRS for brainstem cerebral CMs.[50] The study analyzed 170 patients with 181 CMs treated across 11 hospitals in nine countries, aiming to better understand the risks and benefits of SRS and define its therapeutic role for brainstem CMs. The primary endpoint was symptomatic intracerebral hemorrhage (ICH) rates prior to and after SRS. Secondary outcomes were the occurrence and evolution of neurologic deficit, and adverse effects from radiation. With a median follow-up of 3.4 years, the overall difference in annual hemorrhage rate after SRS was significantly reduced from 14.8/100 CM-years prior to SRS to 2.3/100 CM-years after treatment (-6.4/100 CM-years, 95% CI 3.87 to 11.13, p<0.0001). Multivariate analysis also found a significant reduction in repeat hemorrhage risk (HR 0.17, 95% CI 0.09 to 0.34, p<0.001). Regarding safety, radiation-related adverse effects occurred in nine (5.3%) participants, with T2 hyperintensity being most common. Symptomatic adverse effects were seen in four (2.2%) patients, while new neurologic deficits developed in 27 (15.9%) of participants, and 12 (7.1%) experienced permanent deficits. Overall clinical outcomes showed improvement in 42.3% of patients, stability in 49.7%, and worsening neurologic status in 8.0%, with 5.6% having a worse clinical status at final follow-up. The authors concluded that while SRS significantly reduces rebleeding risk for brainstem CMs, it carries a 5.6% rate of permanent complications. The study's retrospective design represents a key limitation in interpreting these findings.

Phuong (2017) reported on a case series of 79 patients with symptomatic cerebral cavernomas treated with SRS.[51] Complete response, partial response, and stable disease

(best response) were reported in 17%, 82%, and 2%, respectively, of the 60 patients with headache. Complete response, partial response, and stable disease were reported in 31%, 64%, and 5% of the 39 patients with seizures. Complete response, partial response, stable disease, progression, and pseudoprogression were reported in 6%, 75%, 15%, 1%, and 5% of all patients, respectively, with respect to the size of cavernomas at 15 months. Four patients developed recurrent seizures after one year and five patients experienced bleeding within two years after SRS.

A 2014 case series by Lee reported on 31 patients who were treated with SRS for CMs.[52] Treatment followed a single symptomatic bleed in 31 patients (group A) and two or more symptomatic bleeds in 18 patients (group B). The annual hemorrhage rate following SRS within the first two years and after two years (up to a mean follow-up of 64 months) was 7.06% and 2.03% for group A and 9.84% and 1.50% for group B, respectively. Pretreatment hemorrhage rate was 38.36% for group B. Adverse events were reported in four patients, one of which did not resolve during the trial.

A case series of 30 patients treated with SRS for single or multiple CMs was reported by Huang in 2006.[53] For six patients, radiosurgery was for residual lesions identified following[54] craniotomy. Mean follow-up was 59.9 months. Of the 13 patients presenting with seizures, following SRS eight were seizure-free, three had rare episodes of seizures, and two continued to have seizures. Hemorrhage rate pretreatment for the 22 patients presenting initially as acute hemorrhage was 1.9%. For all 30 patients, posttreatment hemorrhage rate was 1.9%. Posttreatment edema was observed in two patients.

Section Summary

The evidence related to the use of SRS for cavernous malformations consists of systematic reviews, one comparative study that utilized consecutive enrollment, and non-randomized studies. The majority of studies report improvements in hemorrhage rates and seizure activity, with low rates of adverse effects from SBRT.

DURAL ARTERIOVENOUS FISTULAS

Singh (2022) published a systematic review and meta-analysis of 21 studies involving 706 patients with dural arteriovenous fistula (dAVF) treated with SRS.[54] Median clinical follow-up was 2.75 years (range 3.8 months to 15.5 years). Nineteen studies with 688 dAVFs included data on complete obliteration (CO) rates. The pooled CO rate was 68.6% (95% CI 60.7% to 76.5%). Thirteen studies with 452 patients included data on symptom improvement. The pooled symptom improvement rate was 97.2% (95% CI 93.2% to 100%). Eight studies with 390 patients reported symptom cure rates. The pooled symptom cure rate after SRS was 78.8% (95% CI 69.3% to 88.2%). Significant heterogeneity was noted for studies including CO rates, symptom improvement, and symptom cure rate. Twelve studies with 283 patients included data on post-SRS permanent neurological deficit (PND) rates. The pooled PND rate after SRS was 1.3% (95% CI 0.8% to 1.8%). There was no significant heterogeneity in the studies reporting PND rates. The authors note that all included studies were retrospective and the analysis has significant risk of bias. Importantly, previous treatment for dAVF, especially embolization, was not controlled for, and the authors were unable to adequately compare SRS alone to multimodality treatment.

OTHER INDICATIONS

SRS has been used for other indications, including rare tumors gamma ventral capsulotomy for obsessive compulsive disorder, and cluster headache. The evidence for these other indications is limited in volume and in quality.[55-57]

PRACTICE GUIDELINE SUMMARY

NATIONAL COMPREHENSIVE CANCER NETWORK

The National Comprehensive Network (NCCN) provides guidelines for cancer treatment by site that include the use of SRS and SBRT for certain cancers.[58-60]

Cancer Site	Tumor Type	Recommendation	Version
Bone	Chondrosarcoma Chordoma	Specialized techniques, such as intensity-modulated RT (IMRT); particle beam RT with protons, carbon ions, or other heavy ions; or stereotactic radiosurgery (SRS) should be considered as indicated in order to allow high-dose therapy while maximizing normal tissue sparing. Consider use of SRS/SBRT, especially for oligometastases.	1.2027
CNS	Adult intracranial and spinal ependymoma – spine or brain reccurrence	• Resection with radiotherapy if no prior radiotherapy; consider use of SRS if geometrically favorable. • If unresectable, radiotherapy if no prior radiotherapy; consider use of SRS if geometrically favorable.	3.2026
CNS	Glioma: Reirradiation	Highly focal techniques like intensity-modulated RT (IMRT), proton therapy, or SRS may be required in reirradiation settings in order to improve dose distribution to critical structures and reduce overlap with prior radiation fields. Treatment may be performed with highly focused modern SRS techniques for lower volume disease; fractionated IMRT, including doses of 35 Gy in 10 fractions for recurrent glioblastoma, and proton therapy to help spare previously irradiated normal brain.	3.2026
CNS	Meningiomas	Observe (preferred for small [≤3 cm] asymptomatic tumors; not generally recommended for symptomatic tumors), or surgery (consider adjuvant RT) or RT. Adjuvant RT and primary RT may be with SRS or fractionated SRS. Stereotactic or image-guided therapy is recommended when using tight margins or when close to critical structures. Consider clinical trial for cases that are not surgically accessible but for which treatment with RT and/or systemic therapy is considered.	3.2026
CNS	Limited Brain Metastases, primary treatment	For newly diagnosed or stable systemic disease, treatment options include SRS (preferred) and WBRT (HA [hippocampal avoidance]-WBRT with memantine if eligible). When patients are managed with SRS, NCCN does ot recommend the routine addition of WBRT as this approach has been consistently associated with cognitive deterioration and no difference in survival..	3.2026
CNS	Limited Brain Metastases, recurrence	• If local recurrence and previous surgery only, options include surgery followed by SRS or RT to the surgical bed and single dose or fractionated stereotactic RT (category 2A) • If local recurrence after radiation, options include surgery followed by SRS or RT to the surgical bed, laser interstitial thermal therapy (LITT), SRS, HA-WBRT, or considering systemic therapy.	3.2026

Cancer Site	Tumor Type	Recommendation	Version
		• If distant brain recurrence and limited brain metastases, options include surgery followed by SRS to the surgical bed, SRS, HA-WBRT, WBRT, or considering systemic therapy.	
CNS	Extensive Brain Metastases, primary treatment	Surgery or SRS or HA-WBRT + memantine OR WBRT without HA +/- memantine or systemic therapy.	3.2026
CNS	Leptomeningeal Metastases	Consider involved-field RT (e.g., partial or WBRT, skull base RT, focal spine RT) to bulky disease for focal disease control and to neurologically symptomatic or painful sites. Consider craniospinal irradiation (CSI) for CNS and CSF disease control in select patients with or without symptoms.	3.2026
Uveal Melanoma	Primary treatment	SRS is an option for tumors with: • Largest diameter >19mm (any thickness) OR • Thickness >10mm (any diameter) OR • Thickness >8mm with optic nerve involvement (any diameter). SRS is the least often used form of definitive radiotherapy for the treatment of primary or recurrent intraocular tumors.	1.2025

NCCN Categories

- **Category 1:** Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- **Category 2A:** Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- **Category 2B:** Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- **Category 3:** Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

*All recommendations are category 2A unless otherwise noted.

AMERICAN SOCIETY FOR RADIATION ONCOLOGY (ASTRO)

Central Nervous System

- ASTRO, the American Society of Clinical Oncology (ASCO), and the Society for Neuro-Oncology (SNO) published 2022 guidelines on the treatment of brain metastases that include the following recommendations:[61]
    - Radiation therapy should not be offered to patients with asymptomatic brain metastases who have:
        - Performance status Karnofsky Performance Status (KPS) ≤ 50 or less, or
        - Performance status KPS < 70 and no systemic therapy options (Type: evidence-based; Evidence quality: low; Strength of recommendation: moderate).
    - SRS alone (as opposed to WBRT or combination of WBRT and SRS) should be offered to patients with one to four unresected brain metastases, excluding small-cell carcinoma. (Type: evidence-based; Evidence quality: intermediate; Strength of recommendation: moderate).
    - SRS alone should be offered to patients with one to two resected brain metastases if the surgical cavity can be safely treated and considering the extent of remaining intracranial disease. (Type: evidence-based; Evidence quality: intermediate; Strength of recommendation: moderate)
    - SRS, WBRT, and the combination of SRS plus WBRT are all reasonable options for patients with more than four unresected or more than two resected brain metastases and better performance status (eg, KPS ≥ 70). SRS may be

preferred for patients with better prognosis or where systemic therapy that is known to be active in the CNS is available (Type: informal consensus; Evidence quality: low; Strength of recommendation: weak).

IDH-Mutant Grade 2 and Grade 3 Diffuse Glioma

SRS is included as an optimal RT technique and field design for adult patients with IDH-mutant grade 2 and grade 3 diffuse glioma.[62]

Grade 4 Adult-type Diffuse Glioma[63]

SRS is included as an appropriate dose-fractionation regimen for RT after biopsy/resection in patients with WHO grade 4 adult-type diffuse glioma (high-grade glioma/astrocytoma, IDH-wildtype glioma, glioblastoma, WHO grade 4 diffuse glioma, WHO grade 4 IDH-mutant diffuse glioma/astrocytoma).

SRS and stereotactic radiation therapy (SRT) are included as appropriate techniques for reirradiation in patients with WHO grade 4 adult-type glioma whose disease recurs following completion of standard first-line therapy.

AMERICAN HEART ASSOCIATION SCIENTIFIC STATEMENT

In 2017, the American Heart Association and American Stroke Association published a scientific statement on the management of brain arteriovenous malformations (AVMs).[64] The statement concludes that the available literature supports the use of SRS for small- to moderate volume brain AVMs that are generally 12 cm^3 of less in volume or located in deep or eloquent regions of the brain.

AMERICAN ACADEMY OF NEUROLOGY

The American Academy of Neurology published evidence-based recommendations in the Treatment of Essential Tremor Practice Parameter in 2005 (updated in 2011 and reaffirmed in 2022).[65, 66] It states, “There is insufficient evidence regarding the surgical treatment of head and voice tremor and the use of gamma knife thalamotomy (Level U).”

CONGRESS OF NEUROLOGICAL SURGEONS

The Congress of Neurological Surgeons published 2019 evidence-based guidelines on “Use of Stereotactic Radiosurgery in the Treatment of Adults with Metastatic Brain Tumors.” These guidelines make the following level 3 recommendations regarding SRS:

- SRS is recommended as an alternative to surgical resection in solitary metastases when surgical resection is likely to induce new neurological deficits, and tumor volume and location are not likely to be associated with radiation-induced injury to surrounding structures.
- SRS should be considered as a valid adjunctive therapy to supportive palliative care for some patients with brain metastases when it might be reasonably expected to relieve focal symptoms and improve functional quality of life in the short term if this is consistent with the overall goals of the patient.
- After open surgical resection of a solitary brain metastasis, SRS should be used to decrease local recurrence rates.

- For patients with solitary brain metastasis, SRS should be given to decrease the risk of local progression.
- For patients with 2 to 4 brain metastases, SRS is recommended for local tumor control, instead of whole brain radiotherapy, when their cumulative volume is < 7 mL.
- The use of stereotactic radiosurgery alone is recommended to improve median overall survival for patients with more than 4 metastases having a cumulative volume < 7 mL.

In 2021, the Congress of Neurological Surgeons published updated guidelines on the treatment of recurrent glioblastoma in adults with radiotherapy.[67] These guidelines provide the following Level III recommendation: “When the target tumor is amenable for additional radiation, re-irradiation is recommended as it provides improved local tumor control, as measured by best imaging response. Such re-irradiation can take the form of conventional fractionation radiotherapy, fractionated radiosurgery, or single fraction radiosurgery.”

INTERNATIONAL STEREOTACTIC RADIOSURGERY SOCIETY

The International Stereotactic Radiosurgery Society (ISRS) has published a variety of relevant clinical practice guidelines and practice opinions related to SRS. For select guidelines, recommendations are based on a ranking of evidence quality with a corresponding strength of recommendation rating scheme:

Strength of Evidence

- Class I:
    - High quality randomized trial with statistically significant difference or no statistically significant difference but narrow confidence intervals
    - Systematic review of Class I RCTs (and study results were homogenous)
- Class II:
    - Lesser quality (eg, <80% follow-up, no blinding, or improper randomization
    - Prospective comparative study
    - Systematic review of Class II studies or Class I studies with inconsistent results
    - Case control study
    - Retrospective comparative study
- Class III:
    - Case series
    - Expert Opinion

Strength of Recommendation

- Level I: High degree of clinical certainty (Class I evidence or overwhelming Class II evidence)
- Level II: Clinical certainty (Class II evidence or a strong consensus of Class III evidence)
- Level III: Clinical uncertainty (Inconclusive or conflicting evidence or opinion)

Recommendations and conclusions from various ISRS guidelines and practice opinions include:

Intracranial noncavernous sinus benign meningioma: Current literature supporting SRS for this condition "lacks level I and II evidence. However, when summarizing the large number of

level III studies, it is clear that SRS can be recommended as an effective evidence-based treatment option (recommendation level II) for grade 1 meningioma.[68]

Non-functioning pituitary adenomas: SRS is an effective and safe treatment for patients with non-functioning pituitary adenomas via consensus opinion.[69] The position paper states that "encouraging short-term data support hypofractionated stereotactic radiotherapy for select patients, and mature outcomes are needed before definitive recommendations can be made."

Benign (World Health Organization Grade I) cavernous sinus meningiomas: Current literature is "limited to level III evidence with respect to outcomes of SRS in patients with cavernous sinus meningiomas. Based on the observed results, SRS offers a favorable benefit to risk profile for patients with cavernous sinus meningioma."[70]

Arteriovenous malformations: Current literature cautiously suggests that "SRS appears to be a safe, effective treatment for grade I-II arteriovenous malformation and may be considered a front-line treatment, particularly for lesions in deep or eloquent locations." However, the literature is "low quality, limiting interpretation."[71]

In 2024, ISRS published a practice guideline on SRS for intermediate (III) or High (IV-V) Spetzler-Martin Grade AVMs using Center for Evidence-Based Medicine (CEBM) levels of evidence.[72] The recommendations are:

- SRS is a safe, effective treatment for Grade III-V AVM (CEBM evidence level 2b).
- SRS should be considered among the front-line management strategies for Grade III-V AVM, alongside observation and microsurgery (CEBM evidence level 2b).
- SRS may be preferred as the primary therapy for those Grade III AVM deemed less favorable for resection (e.g., IIIb/IIIc) (CEBM evidence level 2b).
- SRS may be preferred as the primary therapy in Grade IV-V AVM, absent a configuration of features deemed optimal for resection (CEBM evidence level 2b).
- SRS is likely the preferred adjuvant therapy Grade III-V AVM following incomplete resection, or in patients with medical comorbidities limiting surgical candidacy (CEBM evidence level 4).
- Risk of post-SRS radiation induced complications is increased for high-grade AVMs, which appears to be predominantly a function of AVM volume and dose. This risk may be mitigated via treatment planning that limits the overall and non-AVM 12-Gy volumes (CEBM evidence level 4).
- For larger intermediate-grade and high-grade AVMs, volume staged SRS techniques warrant consideration, as they appear to increase obliterative rates and decrease radiation induced complications without a significant increase in the risk of hemorrhage during the latency period (CEBM evidence level 4).

Cavernous Sinus Hemangioma: "We recommend a dose of 12-16 Gy in 1 fraction for tumor control."[73]

Intracranial Cavernous Malformation (ICM):

- For patients with a surgically inaccessible or eloquently situated ICM with previous symptomatic hemorrhage, SRS is recommended with the intent of reducing the risk of subsequent hemorrhage (Conditional recommendation; Low quality of evidence).

- For patients with ICM causing epilepsy with poor medication control, SRS should be considered with the intent of improving seizure control (Conditional recommendation; Low quality of evidence).
- SRS is not typically recommended for asymptomatic ICM (Moderate recommendation; Low quality of evidence).
- Stereotactic magnetic resonance imaging (MRI) with T2 weighted and gradient echo sequences is recommended for SRS dose planning (Conditional recommendation; Low quality of evidence).
- SRS targeting should include the endothelial wall but exclude the hemosiderin rim and any associated developmental venous anomaly (Conditional recommendation; Low quality of evidence).
- Single fraction SRS prescription doses should range from 11-13 Gy (Conditional recommendation; Low quality of evidence).[43]

Epilepsy: Current literature states that "radiosurgery is an efficacious treatment to control seizures in mesial temporal lobe epilepsy, possibly resulting in superior neuropsychological outcomes and quality of life metrics in selected subjects compared to microsurgery."[12]

Tremor: For medically refractory tremor, "SRS to the unilateral thalamic ventral intermediate nucleus, with a dose of 130 to 150 Gy, is a well-tolerated and effective treatment....and one that i recommended by the International Stereotactic Radiosurgery Society."[18]

Trigeminal neuralgia: Current literature is "limited in its level of evidence, with only 1 comparative randomized trial reported to date. At present, one can conclude that stereotactic radiosurgery is a safe and effective therapy for drug-resistant trigeminal neuralgia."[74]

Dural arteriovenous fistulas: SRS is recommended for patients with "complex dural arteriovenous fistula who are planned for embolization and are at high risk for not achieving complete obliteration with embolization alone; dural arteriovenous fistula who have received previous embolization without complete obliteration and have refractory symptoms; high-risk noncavernous sinus dural arteriovenous fistula or symptomatic cavernous sinus dural arteriovenous fistula who are not candidates for or have refused both embolization or microsurgery."[54]

Vestibular schwannoma:

- Single fraction SRS may be considered for vestibular schwannoma ≥2.5cm in maximum diameter, and/or Koos Grade IV as either the primary treatment modality or for post-operative/recurrent tumor.[75]
- For large vestibular schwannomas, upfront SRS should be considered as opposed to observation due to the potential to optimize long-term local control and within 3-6 months following subtotal resection (Conditional recommendation; Level of evidence: III).[76]
- Sporadic intracanalicular vestibular schwannoma: Upfront SRS should be proposed irrespective of hearing status. SRS results in better rates of tumor control and equivalent hearing preservation compared to conservative surveillance**.** SRS or conservative surveillance or microsurgery can be considered for elderly patients (>80 years).[77]

SUMMARY

Medically Necessary

There is enough research to show that use of stereotactic radiosurgery (SRS) and stereotactic body radiation therapy (SBRT) of intracranial, skull base, and orbital sites for initial treatment or treatment of recurrence improves health outcomes for the following conditions: primary neoplasms of the central nervous system; metastasis to CNS with adequate performance score; arteriovenous malformations; chordomas and chondrosarcomas of the skull base; cavernous malformations, craniopharyngiomas; drug-resistant epilepsy when criteria are met; head and neck cancers when reirradiation is delivered; hemangioblastoma; hemangiopericytoma; glomus jugulare and glomus tympanicum tumors; meningiomas; pituitary adenomas; schwannomas; trigeminal neuralgia that is refractory to medical management; and uveal melanoma. In addition, clinical practice guidelines recommend the use of SRS or SBRT for many of these indications. Therefore, the use of SRS and SBRT may be considered medically necessary when policy criteria are met for these indications.

Investigational

For all other tumors or indications when policy criteria are not met, there is not enough research to show that stereotactic radiosurgery (SRS) or stereotactic body radiation therapy (SBRT) of intracranial, skull base, and orbital sites leads to improved health outcomes. Therefore, SRS and SBRT of intracranial, skull base, and orbital sites is considered investigational when policy criteria are not met.

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CODES

NOTE: Coding for stereotactic radiosurgery typically consists of a series of CPT codes describing the individual steps required; medical radiation physics, clinical treatment planning, attachment of stereotactic head frame, treatment delivery and clinical treatment management.

The correct code to use for image fusion performed to provide enhanced delineation of target and normal critical structures is CPT code 77399 (Unlisted procedure, medical radiation physics, dosimetry and treatment devices, and special services); however, it is considered part of the treatment planning.

Treatment Planning Services:

Treatment delivered with LINAC based MLC may involve planning with the following codes.

Codes	Number	Description
CPT	77301	Intensity modulated radiotherapy plan, including dose volume histograms for target and critical structure partial tolerance specification
	77338	Multi-leaf collimator (MLC) device(s) for intensity modulated radiation therapy (IMRT), design and construction per IMRT plan

NOTE: Treatment delivery:

The codes used for treatment delivery will depend on the energy source used, typically either photons or protons.

Codes	Number	Description
CPT	32701	Thoracic target(s) delineation for stereotactic body radiation therapy (SRS/SBRT), (photon or particle beam), entire course of treatment
	77371	Radiation therapy delivery, stereotactic radiosurgery (SRS), complete course of treatment of cranial lesion(s) consisting of 1 session; multi-source Cobalt 60 based
	77372	Radiation therapy delivery, stereotactic radiosurgery (SRS), complete course of treatment of cranial lesion(s) consisting of 1 session; linear accelerator based
	77373	Stereotactic body radiation therapy, treatment delivery, per fraction to 1 or more lesions, including image guidance, entire course not to exceed 5 fraction
	77435	Stereotactic body radiation therapy, treatment management, per treatment course, to 1 or more lesions, including image guidance, entire course not to exceed 5 fractions

NOTE: Codes for treatment delivery primarily reflects the cost related to the energy source used, and not physician work.

Clinical treatment management:

Codes	Number	Description
CPT	61796	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); 1 simple cranial lesion
	61797	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); each additional cranial lesion, simple (List separately in addition to code for primary procedure)
	61798	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); 1 complex cranial lesion
	61799	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); each additional cranial lesion, complex (List separately in addition to code for primary procedure)
	61800	Application of stereotactic headframe for stereotactic radiosurgery (List separately in addition to code for primary procedure)
	63620	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); 1 spinal lesion
	63621	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); each additional spinal lesion (List separately in addition to code for primary procedure)
	77432	Stereotactic radiation treatment management of cerebral lesion(s) (complete course of treatment consisting of one session.)
HCPCS	G0339	Image guided robotic linear accelerator-based stereotactic radiosurgery, complete course of therapy in one session, or first session of fractionated treatment.
	G0340	Image guided robotic linear accelerator-based stereotactic radiosurgery, delivery including collimator changes and custom plugging, fractionated treatment, all lesions, per session, second through fifth sessions, maximum five sessions per course of treatment
	G0563	Stereotactic body radiation therapy, treatment delivery, per fraction to 1 or more lesions, including image guidance and real-time positron emissions-based delivery adjustments to 1 or more lesions, entire course not to exceed 5 fractions

APPENDIX I: WHO Classification of Tumors of the Central Nervous System	
Gliomas, glioneuronal tumors, and neuronal tumors	**Cranial and paraspinal nerve tumors**
Adult-type diffuse gliomas	Schwannoma
Astrocytoma, IDH-mutant	Neurofibroma
Oligodendroglioma, IDH-mutant, and 1p/19q-codeleted	Perineurioma
Glioblastoma, IDH-wildtype	Hybrid nerve sheath tumor
Pediatric-type diffuse low-grade gliomas	Malignant melanotic nerve sheath tumor
Diffuse astrocytoma, *MYB*- or *MYBL1*-altered	Malignant peripheral nerve sheath tumor
Angiocentric glioma	Paraganglioma
Polymorphous low-grade neuroepithelial tumor of the young	**Meningioma**
Diffuse low-grade glioma, MAPK pathway-altered	**Mesenchymal, non-meningothelial tumors**
Pediatric-type diffuse high-grade gliomas	Soft tissue tumors
Diffuse midline glioma, H3 K27-altered	Fibroblastic and myofibroblastic tumors
Diffuse hemispheric glioma, H3 G34-mutant	Solitary fibrous tumor
Diffuse pediatric-type high-grade glioma, H3-wildtype and IDH-wildtype	Vascular tumors
Infant-type hemispheric glioma	Hemangiomas and vascular malformations
Circumscribed astrocytic gliomas	Hemangioblastoma
Pilocytic astrocytoma	Skeletal muscle tumors
High-grade astrocytoma with piloid features	Rhabdomyosarcoma
Pleomorphic xanthoastrocytoma	Uncertain differentiation
Subependymal giant cell astrocytoma	*Intracranial mesenchymal tumor, FET-CREB fusion-positive*
Chordoid glioma	*CIC*-rearranged sarcoma
Astroblastoma, *MN1*-altered	Primary intracranial sarcoma, *DICER1*-mutant
Glioneuronal and neuronal tumors	Ewing sarcoma
Ganglioglioma	Chondro-osseous tumors
Desmoplastic infantile ganglioglioma / desmoplastic infantile astrocytoma	Chondrogenic tumors
Dysembryoplastic neuroepithelial tumor	Mesenchymal chondrosarcoma
Diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters	Chondrosarcoma
Papillary glioneuronal tumor	Notochordal tumors
Rosette-forming glioneuronal tumor	Chordoma (including poorly differentiated chordoma)
Myxoid glioneuronal tumor	**Melanocytic tumors**
Diffuse leptomeningeal glioneuronal tumor	Diffuse meningeal melanocytic neoplasms
Gangliocytoma	Meningeal melanocytosis and meningeal melanomatosis

APPENDIX I: WHO Classification of Tumors of the Central Nervous System	
Multinodular and vacuolating neuronal tumor	Circumscribed meningeal melanocytic neoplasms
Dysplastic cerebellar gangliocytoma (Lhermitte-Duclos disease)	Meningeal melanocytoma and meningeal melanoma
Central neurocytoma	**Hematolymphoid tumors**
Extraventricular neurocytoma	Lymphomas
Cerebellar liponeurocytoma	CNS lymphomas
Ependymal tumors	Primary diffuse large B-cell lymphoma of the CNS
Supratentorial ependymoma	Immunodeficiency-associated CNS lymphoma
Supratentorial ependymoma, *ZFTA* fusion-positive	Lymphomatoid granulomatosis
Supratentorial ependymoma, *YAP1* fusion-positive	Intravascular large B-cell lymphoma
Posterior fossa ependymoma (multiple subtypes)	Miscellaneous rare lymphomas in the CNS
Spinal ependymoma (multiple subtypes)	MALT lymphoma of the dura
Myxopapillary ependymoma	Other low-grade B-cell lymphomas of the CNS
Subependymoma	Anaplastic large cell lymphoma (*ALK*+/*ALK*−)
Choroid plexus tumors	T-cell and NK/T-cell lymphomas
Choroid plexus papilloma	Histiocytic tumors
Atypical choroid plexus papilloma	Erdheim-Chester disease
Choroid plexus carcinoma	Rosai-Dorfman disease
Embryonal tumors	Juvenile xanthogranuloma
Medulloblastoma	Langerhans cell histiocytosis
Medulloblastomas, molecularly defined (multiple types)	Histiocytic sarcoma
Medulloblastomas, histologically defined	**Germ cell tumors**
Other CNS embryonal tumors	Teratoma (multiple types)
Atypical teratoid/rhabdoid tumor	Germinoma
Cribriform neuroepithelial tumor	Embryonal carcinoma
Embryonal tumor with multilayered rosettes	Yolk sac tumor
CNS neuroblastoma, *FOXR2*-activated	Choriocarcinoma
CNS tumor with *BCOR* internal tandem duplication	Mixed germ cell tumor
CNS embryonal tumor	**Tumors of the sellar region**
Pineal tumors	Adamantinomatous craniopharyngioma
Pineocytoma	Papillary craniopharyngioma
Pineal parenchymal tumor of intermediate differentiation	Pituicytoma, granular cell tumor of the sellar region, and spindle cell oncocytoma
Pineoblastoma	Pituitary adenoma/PitNET

APPENDIX I: WHO Classification of Tumors of the Central Nervous System	
Papillary tumor of the pineal region	Pituitary blastoma
Desmoplastic myxoid tumor of the pineal region, *SMARCB1*-mutant	**Metastases to the CNS**
	Metastases to the brain and spinal cord parenchyma
	Metastases to the meninges

Adapted from Louis (2021).[78]

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